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NEWS 3	Feb 06	Engineering Information Encompass files have new names
NEWS 4	Feb 16	TOXLINE no longer being updated
NEWS 5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS 6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7	May 07	DGENE Reload
NEWS 8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS 9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI
NEWS 10	Aug 23	In-process records and more frequent updates now in MEDLINE
NEWS 11	Aug 23	PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
NEWS 12	Aug 23	Adis Newsletters (ADISNEWS) now available on STN
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NEWS 14	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS 15	Oct 09	Number of Derwent World Patents Index updates increased
NEWS 16	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 17	Oct 22	Over 1 million reactions added to CASREACT
NEWS 18	Oct 22	DGENE GETSIM has been improved

NEWS EXPRESS	August 15 CURRENT WINDOWS VERSION IS V6.0c, CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP), AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

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DICTIONARY FILE UPDATES:  22 OCT 2001  HIGHEST RN 364037-88-7

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Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s valsartan/CN
L1             1 VALSARTAN/CN

=> s L1
L2             1 VALSARTAN/CN

=> file caplus
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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         8.22       8.37

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FILE COVERS 1947 - 24 Oct 2001  VOL 135 ISS 18
FILE LAST UPDATED: 22 Oct 2001  (20011022/ED)

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The CA Lexicon is now available in the Controlled Term (/CT) field. Enter HELP LEXICON for full details.


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=> s l1
L3          233 L1

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         530668 STRUCTURES
        2258454 STRUCTURE
                  (STRUCTURE OR STRUCTURES)
L4            9 L3 AND STRUCTURE

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L4   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:311121  CAPLUS
DOCUMENT NUMBER:          135:251404
TITLE:                    Does protein binding modulate the effect of
                          angiotensin II receptor antagonists?
AUTHOR(S):                Maillard, Marc P.; Centeno, Catherine;
                          Frostell-Karlsson, Asa; Brunner, Hans R.; Burnier,
                          Michel
CORPORATE SOURCE:         Division of Hypertension and Vascular Medicine,
                          Lausanne University Hospital, Lausanne, CH-1011,
                          Switz.
SOURCE:                   JRAAS (2001), 2(Suppl. 1), S54-S58
                          CODEN: JRAAAG; ISSN: 1470-3203
PUBLISHER:                JRAAS Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Angiotensin II AT1-receptor antagonists are highly bound to blood plasma
     proteins (.gtoreq. 99%). With some antagonists, such as DuP-532, the
     protein binding was such that no efficacy of the drug could be
     demonstrated clin. Whether protein binding interferes with the efficacy
     of other antagonists is not known. The authors have therefore
     investigated in vitro how plasma proteins may affect the antagonistic
     effect of different AT1-receptor antagonists. A radio-receptor binding
     assay was used to analyze the interaction between proteins and the
ability
     of various angiotensin II (Ang II) antagonists to block AT1-receptors.
In
     addn., the Biacore technol., a new technique which enables the real-time
     monitoring of binding events between 2 mols., was used to evaluate the
     dissocn. rate consts. of 5 AT1-receptor antagonists from human serum
     albumin. The in vitro AT1-antagonistic effects of different Ang II
     receptor antagonists were differentially affected by the presence of
human
```

plasma, with rightward shifts of the IC50 ranging from 1 to several orders of magnitude. The importance of the shift correlates with the dissocn. rate consts. of these drugs from albumin. The authors' expts. also show that the way that AT1-receptor antagonists bind to proteins differs from 1 compd. to another. These results suggest that the interaction with plasma proteins appears to modulate the efficacy of some Ang II antagonists. Although the high binding level of Ang II receptor antagonist to plasma proteins appears to be a feature common to this class of compds., the kinetics and characteristics of this binding is of great importance. With some antagonists, protein binding interferes markedly with their efficacy to block AT1-receptors.

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REFERENCE COUNT: 12
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:82589 CAPLUS
DOCUMENT NUMBER: 135:86860
TITLE: Antiplatelet action of losartan involves TXA2 receptor
antagonism but not TXA2 synthase inhibition
AUTHOR(S): Chlopicki, S.; Koda, M.; Chabielska, E.; Buczko, W.; Gryglewski, R. J.
CORPORATE SOURCE: Department of Pharmacology Medical College, Jagiellonian University, Pol.
SOURCE: J. Physiol. Pharmacol. (2000), 51(4, Pt. 1), 715-722
CODEN: JPHPEI; ISSN: 0867-5910
PUBLISHER: Polish Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Various AT1 receptor antagonists including losartan are known to inhibit human platelet activation by antagonizing TXA2/PGH2 receptors (TP receptors). Presently, we check a hypothesis that losartan, an imidazole deriv. in contrast with valsartan, a non-imidazole compd., may inhibit human platelet activation also through inhibition of TXA2 synthesis. Inhibitory action of losartan, its active metabolite EXP 3174, and valsartan, on collagen-induced platelet aggregation and TXA2 generation was compared to effects achieved by each compd. on U 46619-induced aggregation in aspirinized platelets. Losartan and aspirin inhibited collagen-induced platelet aggregation with approx. the same potency, whereas EXP 3174 and valsartan showed much weaker antiplatelet effects. Interestingly, losartan, EXP 3174 and valsartan displayed similar potencies as inhibitors of U 46619-induced aggregation in aspirinized platelets as in collagen-induced aggregation in non-aspirinized platelets.

None of the above three AT1 antagonists, up to a concn. of 300 .mu.M, did influence collagen-induced TXA2 synthesis in human platelets. In conclusion, antiplatelet effects of AT1 antagonists, irresp. of the presence or absence of non-condensed imidazole in their chem. **structure**, involve antagonism of TP receptors but not inhibition of TXA2 synthesis in platelets.

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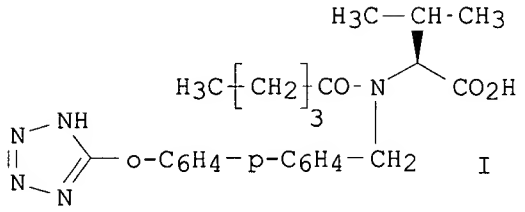
L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:805989 CAPLUS
DOCUMENT NUMBER: 134:101153
TITLE: Carbon-14 labelling of DIOVAN in its valine-moiety
AUTHOR(S): Moenius, Th.; Voges, R.; Burtscher, P.; Zuger, Ch.
CORPORATE SOURCE: Preclinical Safety, DMPK-IL, Novartis Pharma AG, CH-Basel, Switz.
SOURCE: J. Labelled Compd. Radiopharm. (2000), 43(13), 1245-1252
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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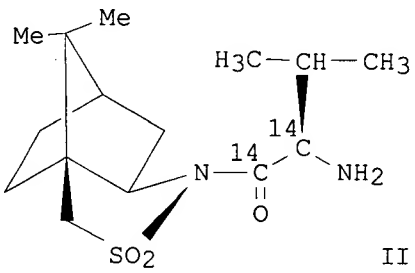

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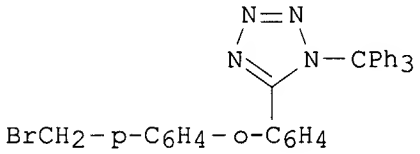

III

AB As a highly specific and non peptide AT1-antagonist Valsartan (I) is marketed under the trade-name DIOVAN for effective treatment of hypertension. This paper describes the synthesis of 14C-labeled I, which incorporates two 14C isotopes in the valine-moiety. Reaction of (-)-bromo-[1,2-14C]acetyl bornane-10.2-sultam ((-)-[14C2]BABS) with benzophenone imine gave (-)-diphenyl-methylene[1,2-14C2]glycinyl bornane-10.2-sultam ((-)-[14C2]DPMGBS), which was alkylated with 2-iodopropane to build-up the valine **structure**. Initially the resulting sultam-protected valine (II) was treated with treated with bromide (III) to produce the precursor. However, under conditions routinely used for sultam-cleavage deprotection resulted in the racemization of the amino acid. Successful cleavage was accomplished via N-Boc-protection of II followed by hydrolytic cleavage of the auxiliary and esterification to give the L-[14C2]valine benzyl ester. Finally [14C2]-I was synthesized in a 10 step synthesis in an overall radiochem. yield of 10% relative to the (-)-[1,2-14C]BABS employed.

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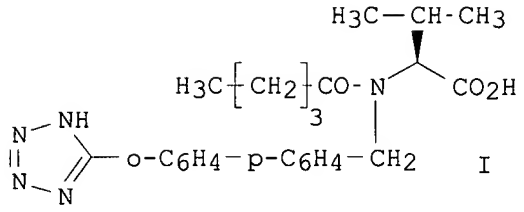

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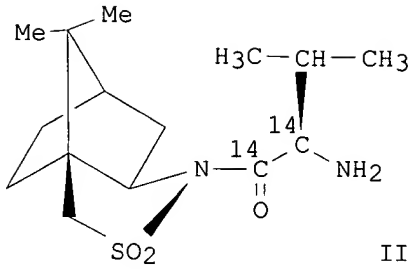

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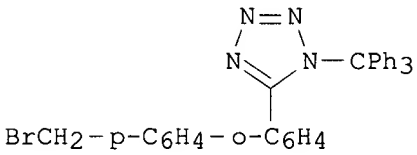

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REFERENCE COUNT: 14
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:476348 CAPLUS
DOCUMENT NUMBER: 133:171982
TITLE: Basilar artery remodelling in the genetically hypertensive rat: effects of nitric oxide synthase

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inhibition and treatment with valsartan and enalapril

AUTHOR(S): Ledingham, J. M.; Laverty, R.
CORPORATE SOURCE: Department of Pharmacology, School of Medical Sciences, University of Otago, Dunedin, N. Z.
SOURCE: Clin. Exp. Pharmacol. Physiol. (2000), 27(8), 642-646
CODEN: CEXPB9; ISSN: 0305-1870
PUBLISHER: Blackwell Science Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1. The **structure** of the basilar artery and the relationship of **structure** to blood pressure and ventricular hypertrophy was examd. in genetically hypertensive (GH) rats, their control normotensive (N) Wistar strain, GH given the nitric oxide synthase (NOS) inhibitor, NG-nitro-L-arginine Me ester (L-NAME) and GH given L-NAME and either valsartan or enalapril. 2. Systolic blood pressure (SBP; tail-cuff) was measured weekly from age 7-12 wk. At the end of the expt. at 12 wk, the basilar artery was fixed by perfusion and embedded in Technovit (Heraeus Kulzer GmbH, Werheim, Germany). Serial sections were cut and stained and stereol. anal. applied to quantify the morphol. of the vessels. Left ventricular (LV) mass was detd. 3. Both SBP and LV mass were significantly increased in GH compared with N ($P < 0.001$) and increased further in GH given L-NAME ($P < 0.05$). The GH L-NAME + valsartan and GH L-NAME + enalapril groups had significantly lower ($P < 0.001$) SBP and LV mass than the GH L-NAME group. 4. Basilar arteries in GH (which are frankly hypertensive, but have no apparent endothelial defect) showed hypotrophic inward remodelling compared with the N control group with no change in media to lumen ratio. 5. In the GH L-NAME group, further inward remodelling occurred and the media to lumen ratio was increased compared with N ($P < 0.01$) and GH ($P < 0.05$). Valsartan treatment in GH L-NAME rats caused eutrophic outward remodelling. Enalapril caused hypertrophic outward remodelling, suggesting that the angiotensin II-stimulated growth was not entirely suppressed with an angiotensin-converting enzyme inhibitor or that there was a bradykinin effect with enalapril. 6. In GH with an endothelial defect induced by treatment with L-NAME, the further remodelling, together with an increased media to lumen ratio and the development of a stroke-like syndrome, indicates the NOS-inhibited GH rat may be a useful model for essential hypertension (where it is known that endothelial abnormalities exist) and where stroke can develop as a consequence of the hypertension.
AB 1. The **structure** of the basilar artery and the relationship of **structure** to blood pressure and ventricular hypertrophy was examd. in genetically hypertensive (GH) rats, their control normotensive (N) Wistar strain, GH given the nitric oxide synthase (NOS) inhibitor, NG-nitro-L-arginine Me ester (L-NAME) and GH given L-NAME and either valsartan or enalapril. 2. Systolic blood pressure (SBP; tail-cuff) was measured weekly from age 7-12 wk. At the end of the expt. at 12 wk, the basilar artery was fixed by perfusion and embedded in Technovit (Heraeus Kulzer GmbH, Werheim, Germany). Serial sections were cut and stained and stereol. anal. applied to quantify the morphol. of the vessels. Left ventricular (LV) mass was detd. 3. Both SBP and LV mass were significantly increased in GH compared with N ($P < 0.001$) and increased further in GH given L-NAME ($P < 0.05$). The GH L-NAME + valsartan and GH L-NAME + enalapril groups had significantly lower ($P < 0.001$) SBP and LV mass than the GH L-NAME group. 4. Basilar arteries in GH (which are frankly hypertensive, but have no apparent endothelial defect) showed hypotrophic inward remodelling compared with the N control group with no change in media to lumen ratio. 5. In the GH L-NAME group, further inward

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REFERENCE COUNT: 27
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:204117 CAPLUS
DOCUMENT NUMBER: 126:195243
TITLE: Method for treating renal disease using an ACE inhibitor and an angiotensin II antagonist
INVENTOR(S): Remuzzi, Giuseppe; Eydelloth, Ronald S.; Owen, Roger A.; Shahinfar, Shahnaz
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Laboratoires Merck Sharp & Dohme-Chibret Snc; Remuzzi, Giuseppe; Eydelloth, Ronald S.; Owen, Roger A.; Shahinfar, Shahnaz
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9702032	A1	19970123	WO 1996-US10942	19960626
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RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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AU 9662916	A1	19970205	AU 1996-62916	19960626
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EP 835106	A1	19980415	EP 1996-921794	19960626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11508894	T2	19990803	JP 1996-505200	19960626

PRIORITY APPLN. INFO.: US 1995-770 19950630
GB 1996-2854 19960213

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WO 1996-US10942 19960626

AB The present invention relates to a method of treating and/or preventing renal disease with the coadministration of an ACE inhibitor and an AII receptor antagonist. The present invention also relates to a method for protection of renal **structure** and/or renal function with the coadministration of an ACE inhibitor an an AII receptor antagonist. The combination is also useful in preventing renal injury and protecting glomerular **structure**. The effect of Lisinopril (ACE inhibitor) and Losartan (angiotensin II receptor antagonist) in animals with diabetic nephropathy is described.

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L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:50392 CAPLUS
DOCUMENT NUMBER: 126:139974
TITLE: A 3D QSAR CoMFA study of non-peptide angiotensin II receptor antagonists
AUTHOR(S): Belvisi, Laura; Bravi, Gianpaolo; Catalano, Giovanna; Mabilia, Massimo; Salimbeni, Aldo; Scolastico, Carlo
CORPORATE SOURCE: Organic and Industrial Chemistry Department, C.N.R. (National Research Council) Centre for the Study of Organic and Natural Compounds, University of Milan, Milan, I-20133, Italy
SOURCE: J. Comput.-Aided Mol. Des. (1996), 10(6), 567-582
CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER: ESCOM
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of non-peptide angiotensin II receptor antagonists was investigated with the aim of developing a 3D QSAR model using comparative mol. field anal. descriptors and approaches. The main goals of the study were dictated by an interest in methodologies and an understanding of the binding requirements to the AT1 receptor. Consistency with the previously derived activity models was always checked to contemporarily test the validity of the various hypotheses. The specific conformations chosen for the study, the procedures invoked to superimpose all **structures**, the conditions employed to generate steric and electrostatic field values and the various PCA/PLS runs are discussed in detail. The effect of exptl. design techniques to select objects (mols.) and variables (descriptors) with respect to the predictive power of the QSAR models derived was esp. analyzed.

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L4 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:29751 CAPLUS
DOCUMENT NUMBER: 126:98857
TITLE: Non-peptide angiotensin II receptor antagonists: PCA & PLS analyses employing different types of 3D molecular descriptors
AUTHOR(S): Mabilia, M.; Fioravanzo, E.
CORPORATE SOURCE: S.IN - Soluzioni Informatiche, Vicenza, I-36100, Italy
SOURCE: Bioact. Compd. Des. (1996), 127-136. Editor(s): Ford, Martyn G. Bios Scientific Publishers: Oxford, UK. CODEN: 63SXAI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Different three-dimensional (3D) mol. descriptors were generated for a set of angiotensin II receptor antagonists with the aim to: a. establish quant. **structure**-activity relationships (QSAR) by means of Principal Component Anal. (PCA) and Partial Least-Squares (PLS) methods, b. compare the modeling and predictive capabilities of the different types of descriptors considered, c. establish the effect of exptl. design techniques to select objects (mols.) and variables (descriptors), with respect to the predictive power of the QSAR models derived.
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L4 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:381984 CAPLUS
DOCUMENT NUMBER: 125:75808
TITLE: Remodelling of resistance arteries in genetically hypertensive rats by treatment with valsartan, an angiotensin II receptor antagonist
AUTHOR(S): Ledingham, Janet M.; Laverty, R.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Otago Med. Sch., Dundein, N. Z.
SOURCE: Clin. Exp. Pharmacol. Physiol. (1996), 23(6/7),

09230817

576-578
CODEN: CEXPB9; ISSN: 0305-1870
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, New Zealand genetically hypertensive (GH) rats were treated with valsartan, a specific angiotensin II (AT1) receptor antagonist, to measure the effects on blood pressure (BP), cardiac hypertrophy and the **structure** of resistance arteries. Normotensive (N) rats were used as controls. Valsartan (val) was given to GH rats at three different doses (10, 3 or 0.3 mg/kg per day, via osmotic mini-pumps implanted i.p.) from age 4-10 wk. Untreated GH (mini-pump + vehicle) and N rats (mini-pump + vehicle) were used as controls. BP was measured weekly and at the end of the expt., left ventricular (LV) mass was recorded and the **structure** of mesenteric resistance arteries (MRA) was detd. using stereol. methods. BP fell in a dose-dependent fashion, being reduced to normotensive levels by 10 mg/kg; LV mass was significantly reduced ($P < 0.0001$) to below normotensive values in the GH group given 10 mg/kg val and significantly reduced ($P < 0.001$), although not normalized, in the other two treatment groups. In MRA, the media/lm (M/L) ratio was reduced by val according to dose level, to below normotensive values in GHval10, and to levels not different from normotensive values in the GHval3 and GHval0.3 groups. The hypertrophy of smooth muscle cells in GH rats was reduced with val treatment at all doses. Reversal of cardiac and vascular hypertrophy occurred even when BP was not reduced to normotensive levels, indicating an effect on vessel growth but without any retardation of body growth. These results suggest that the vascular structural changes seen after val and angiotensin converting enzyme inhibitor treatment are probably due to the blocking of angiotensin rather than any bradykinin effect.

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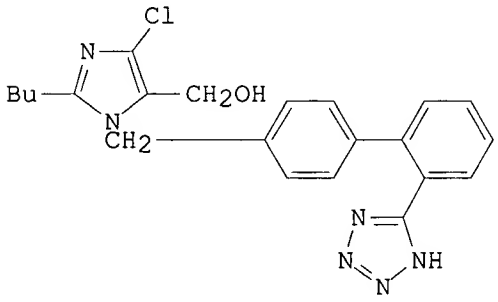
L4 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:260544 CAPLUS
DOCUMENT NUMBER: 120:260544
TITLE: Valsartan, a potent, orally active angiotensin II antagonist developed from the structurally new amino acid series
AUTHOR(S): Buhlmayer, Peter; Furet, Pascal; Criscione, Leoluca; de Gasparo, Marc; Whitebread, Steven; Schmidlin, Tibur; Lattmann, Rene; Wood, Jeanette
CORPORATE SOURCE: Res. Dep., Ciba-Geigy Ltd., Basel, CH-4002, Switz.
SOURCE: Bioorg. Med. Chem. Lett. (1994), 4(1), 29-34
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Starting from the **structure** of DuP-753 (I) and a 3-dimensional model of the pentapeptide Tyr-Ile-His-Pro-Ile, a series of new and highly potent antagonist has been designed where the imidazole moiety of the DuPont compd. has been replaced by an N-acylated aminoacid residue. Valsartan (CGP48933) [(S)-N-valeryl-N-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]valine], has been selected for clin. investigation.

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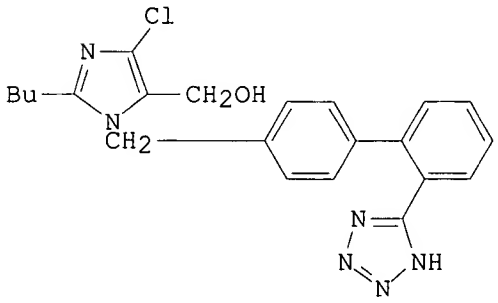

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